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DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Warning Letter

Via Federal Express

Mr. Carl Hull
Chief Executive Officer
Applied Imaging Corporation
2380 Walsh Avenue, Bldg. B
Santa Clara, California 95051

MAR 28 2003

Dear Mr. Hull:

The Food and Drug Administration (FDA) has reviewed a folder of information entitled "It's Time," regarding your firm's ariol SL-50 automated image analysis system (ariol SL-50), distributed at last year's annual meeting of the American Society of Clinical Oncology. FDA has also reviewed your Internet site, http://www.aicorp.com.

The ariol SL-50 is a medical device as defined by Section 201(h) of the Federal Food, Drug, and Cosmetic Act (Act), 21 U.S.C. § 321(h). Specifically, it is an automated scanning microscope and image analysis system. Applied Imaging has one 510(k) on file with FDA for the SlideScan™ automated scanning microscope (K001420), which is intended for *in vitro* diagnostic use as an aid to the pathologist in the detection, classification, and counting of epithelial cells positively stained by immunohistochemistry (IHC) for the presence of cytokeratins in heparinized bone marrow samples. There is no application on file with FDA for the ariol SL-50 device.

The "It's Time" folder, the brochures found within the folder, and information on Applied Imaging's website create intended uses for the ariol SL-50 device which have not been evaluated by FDA. For example, the folder states that the ariol SL-50 system can be used for imaging and scoring the breast cancer related gene (HER-2/neu) IHC and for analyzing the HER-2/neu gene using fluorescent *in situ* hybridization (FISH). The folder also states that the ariol SL-50 can be used for "occult tumor cell detection in bone marrow." A brochure in the folder, entitled "Ariol Imaging Module Panel – 2002," states that the system's Kisight™ module provides "[r]apid image analysis for efficient quantification and scoring of IHC stained tissue for nuclear markers." Another brochure in the folder, entitled "Ariol hersight™," states that this module provides "[h]igh throughput digital analysis and scoring for HER-2/neu expression in IHC stained tissue." Similarly, your website, at http://www.aicorp.com/ariol/features.htm, states that the Hersight™ module "enables membrane specific analysis of IHC staining intensity staining integrity to offer the most complete package of analysis for HER-2/neu IHC." Your website also states that the ariol SL-50 features "Full FISH and IHC Imaging Opportunities."

Your folder, brochures, and website state that the ariol SL-50 is not for use in diagnostic procedures and is for research use only. "Research use only" is a term used to describe products in the initial research phase of development that are not represented as effective *in vitro*

diagnostic products. It is clear from the medical and diagnostic claims made for the ariol SL-50 in your promotional materials that this product is not in the research phase of development.

Accordingly, the ariol SL-50 device is adulterated under section 501(f)(1)(B) of the Act, in that it is a class III device under section 513(f) and you do not have an approved application for premarket approval in effect pursuant to section 515(a) or an approved application for investigational device exemption under section 520(g). This device is also misbranded under section 502(o), because a notice or other information respecting the device was not provided to the FDA as required by section 510(k). For a product requiring premarket approval before marketing, the notification required by section 510(k) of the act is deemed to be satisfied when a premarket approval application (PMA) is pending before the agency. 21 CFR 807.81(b).

This letter is not intended to be an all-inclusive list of deficiencies associated with your device. It is your responsibility to ensure adherence to each requirement of the Act and regulations for every FDA-regulated product that you market. You are responsible for investigating and reviewing all materials to ensure compliance with applicable regulations.

You should take prompt action to correct these violations. Failure to promptly correct these violations may result in regulatory action being initiated by the FDA without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil money penalties. Also, Federal agencies are informed about the Warning Letters we issue, such as this one, so that they may consider this information when awarding government contracts.

Please notify this office in writing within fifteen (15) working days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

Please direct your response to James Woods, Deputy Director of Patient Safety and Product Quality, Office of In Vitro Diagnostic Device Evaluation and Safety, 2098 Gaither Road, HFZ-440, Rockville, Maryland 20850.

Sincerely yours,

S Gutman

Steven I. Gutman
Director
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health